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Impact of age and sex on primary preventive treatment for cardiovascular disease in the West Midlands, UK: cross sectional study

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Abstract

Objectives To establish the impact of age and sex on primary preventive treatment for cardiovascular disease in a typical primary care population.

Design Cross sectional study of anonymised patient records.

Participants All 41 250 records of patients aged ≥40 registered at 19 general practices in the West Midlands, United Kingdom, were extracted and analysed.

Main outcome measures Patients' demographics, risk factors for cardiovascular disease (blood pressure, total cholesterol concentration), and prescriptions for primary preventive drugs were extracted from patients' records. Patients were subdivided into five year age bands up to 85 (patients aged ≥85 were analysed as one group) and prescribing trends across the population were assessed by estimating the proportion of patients prescribed with antihypertensive drug or statin drug, or both, in each group.

Results Of the 41 250 records screened in this study, 36 679 (89%) patients did not have a history of cardiovascular disease and therefore could be considered for primary preventive treatment. The proportion receiving antihypertensive drugs increased with age (from 5% (378/6978) aged 40-44 to 57% (621/1092) aged ≥85) as did the proportion taking statins up to the age of 74 (from 3% (201/6978) aged 40-44 to 29% (675/2367) aged 70-74). In those aged 75 and above, the odds of a receiving prescription for a statin (relative to the 40-44 age group) decreased with every five year increment in age (odds ratio 12.9 (95% confidence interval 10.8 to 15.3) at age 75-79 to 5.7 (4.6 to 7.2) at age ≥85; P<0.001). There were no consistent differences in prescribing trends by sex.

Conclusions Previously described undertreatment of women in secondary prevention of cardiovascular disease was not observed for primary prevention. Low use of statins in older people highlights the need for a stronger evidence base and clearer guidelines for people aged over 75.

Introduction

Cardiovascular disease remains the principal cause of death in the United Kingdom and around the world.[1] Primary and secondary prevention of cardiovascular disease is a high priority, and this is reflected in current guidelines[2 3] and national quality standards.[4] These guidelines are supported by a large body of evidence that promotes the use of drugs to lower blood pressure and cholesterol concentration in patients at high risk of future cardiovascular disease events.[5-10]

It is well established that age and sex inequalities exist in secondary prevention of cardiovascular disease, particularly for cholesterol lowering treatment.[11-17] Previous research has shown a "treatment-risk" paradox for secondary prevention, whereby patients become less likely to receive appropriate treatment the older they get.[11-14] For example, Ko et al, showed that in addition to statin prescription rates being low throughout the secondary prevention population (75 617/396 077, 19%), the likelihood of statin treatment was 6% lower with each year increase in age.[14]

Health inequalities in secondary prevention by sex have also been described.[15 16] Compared with men, women are less likely to be prescribed both antihypertensive (58% of women *v* 62% of men, P<0.001)[15] and lipid lowering drugs (reported variously as 66% *v* 71%, P<0.001[15]; and 50% *v* 67%, P<0.01[16]). These disparities in statin prescription existed despite a higher proportion of women being above the recommended target cholesterol concentration.

The situation for primary prevention is less clear. To our knowledge, no previous studies have assessed the impact of age and sex on prescribing patterns in a primary preventive population. This might be because of the difficulty in defining who is eligible for such treatment when most patients have not

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been adequately screened to allow their absolute cardiovascular disease risk to be assessed.

Optimal screening strategies for identifying patients most at risk of developing cardiovascular disease have been studied extensively.[18-21] It is unclear whether targeted treatment after such screening is more beneficial than blanket treatment for all those without existing cardiovascular disease with a "polypill" approach.[22] In the UK, the Department of Health have opted to introduce a programme of "NHS health checks" for everyone aged between 40-74 without existing cardiovascular disease, aiming to reach all people within this age range over a period of five years.[23] It is intended that people identified as having a high 10 year absolute risk of cardiovascular disease (that is, over 20%) will be provided with support for behaviour change and pharmacological treatment in accordance with relevant guidelines.[3 23]

Concerns about the viability and potential benefits of such a programme have been expressed.[24 25] As one of the main aims of the programme is to reduce health inequalities,[23] it is important to establish whether the age and sex inequalities observed in secondary prevention also exist in primary prevention. We assessed the impact of age and sex on prescription of antihypertensive drugs and statins for primary prevention of cardiovascular disease in a typical primary care population.

Methods

We carried out a cross sectional retrospective study of primary care medical records. We obtained anonymised data from the electronic health records of all patients aged 40 and above registered at 19 general practices across the West Midlands. The practices were purposefully selected to represent different practice sizes and different levels of socioeconomic deprivation by using the indices of multiple deprivation score of the practice area. Relevant data were extracted with MIQUEST software.

Data queries were run from 17 October 2008 to 6 October 2009. Extracted information included demographic data, cardiovascular disease risk factors, and records of prescribed drugs. The presence of data for blood pressure or cholesterol concentration, or both, in the five years before the query date was defined as a non-zero value recorded in a value field linked to a relevant Read code for blood pressure or total cholesterol concentration. We made no attempts to impute missing data. Table 1 shows the proportion of patients with recorded cardiovascular disease risk factors⇓. We extracted data concerning prescription of drugs to lower blood pressure and cholesterol concentration in the 90 days before the query date.

We excluded from our analysis any patients with a history of cardiovascular disease (stroke, transient ischaemic attack, myocardial infarction, coronary artery disease, heart failure, peripheral vascular disease). A history of cardiovascular disease was defined as any patient with a Read code for cardiovascular disease in their medical records. We assumed that, because of quality standards in the UK whereby general practitioners are paid based on accurate recording of information such as this,[4] these data would be sufficiently accurate to identify the true secondary prevention population.

All patients without a history of cardiovascular disease were considered potentially eligible for primary prevention drugs. Strictly, only patients with a high absolute cardiovascular disease risk (≥20%) and no other comorbidities should be considered for primary prevention treatment.[3 26] Calculators used to establish this risk, however, have been validated only in patients aged up to 74,[27-29] and no standardised method of estimating risk in

elderly patients aged 75 and above has been established, though most people in this age group will have an absolute cardiovascular disease risk of ≥20%.[30] To assess primary prevention trends in all eligible age groups, we included all patients aged over 40 with no history of cardiovascular disease, regardless of their calculated risk.

The proportion of patients receiving statins or antihypertensive drugs, or both, was estimated in five year age bands from 40 to 84. Those aged 85 and over were analysed in a single group because five year age bands above this age contained too few patients for reliable analyses between groups.

We used descriptive statistics to identify the proportion of patients with measured information on cardiovascular disease risk factors such as blood pressure, total cholesterol concentration, smoking status, and prescription for an antihypertensive drug or statin. We performed logistic regression analyses to examine associations between age group, sex, and prescription (statin and antihypertensive). Odds ratios were estimated to determine the change in likelihood of prescription of drug treatment per five year increase in age (with prescription rates in the first age group (aged 40-44) used as the reference category). All data are presented as means and standard deviation, odds ratios with 95% confidence interval, and percentages of the total primary prevention population (unless otherwise stated).

Results

Of the 90 516 patients registered at participating practices, 41 250 matched our inclusion criteria (patients aged ≥40). Of these, 4571 (11%) had a record of existing cardiovascular disease, leaving 36 679 patients potentially eligible for primary preventive treatment. Table 1 shows that the proportion of patients with cardiovascular disease increased with age (from 1% (57/7035) at age 40-44 to 37% (632/1724) at age ≥85).

The proportion of patients with some specific risk factors for cardiovascular disease in the primary prevention population decreased with age: there were fewer men, fewer individuals with South Asian/Afro-Caribbean ethnicities, and fewer smokers (table 1). Recording of both blood pressure and cholesterol concentration improved with age, albeit from a much lower baseline for cholesterol. When recorded, mean blood pressure increased with age and mean cholesterol was stable (table 1).

The proportion of patients receiving antihypertensive drugs increased with age (from 5% (378/6978) aged 40-44 to 57% (621/1092) aged ≥85) (fig 1⇓). The likelihood of prescription of an antihypertensive drug increased with each five year increment in age up to ≥85 (from odds ratio 1.8 (95% confidence interval 1.6 to 2.0) at age 45-49 (P<0.001) to 25.8 (22.2 to 30.1) at age 80-84 (P<0.001); table 2⇓).

The proportion of patients taking statin drugs also increased with age up to 74 (from 3% (201/6978) aged 40-44 to 29% (675/2367) aged 70-74) (fig 2⇓). In those aged 75 and over, however, only 963/4254 (23%) were prescribed statins (fig 2⇓). The likelihood of prescription of a statin was consistently higher with each five year increment in age up to 74 (from 1.8 (1.5 to 2.1) at age 45-49 (P<0.001) to 13.6 (11.5 to 16.1) at age 70-74 (P<0.001); table 2). Thereafter, in those aged ≥75, the odds of receiving a statin prescription decreased with every five year increment in age (from 12.9 (10.8 to 15.3) at age 75-79 (P<0.001) to 5.7 (4.6 to 7.2) at age ≥85 (P<0.001)).

The proportion of men and women prescribed antihypertensive drugs was similar in all age groups apart from those aged 65-69 and 75-79, in whom prescriptions were more common in women

(39% (610/1562) in women *v* 34 % (454/1331) in men for ages 65-69; 55% (634/1152) *v* 48 % (367/757), respectively, for ages 75-79; fig 3⇓). Overall, women were 10% more likely to receive antihypertensive drugs than men (P<0.001). Statin prescriptions were more common in men than women in those aged under 60 (6% (663/11 078) in women *v* 8% (947/11 892) in men for ages 40-59) but higher in women aged over 75 (28% (537/1949) in women *v* 22% (272/1213) in men, for ages 75-84). Overall, men were more likely to receive statin prescriptions than women (odds ratio 1.1, 1.1 to 1.2; P<0.001).

Discussion

Summary of findings

This study assessed current rates of prescription of primary prevention across a typical primary care population with no previous history of cardiovascular disease. As expected, blood pressure increased with age but while antihypertensive treatment also increased, many older people did not receive blood pressure lowering drugs and most people of all ages were not prescribed statins. This was particularly an issue in the oldest age groups where, despite reasonable recording of risk factors, statins were prescribed in only a fraction of those eligible assuming an absolute cardiovascular disease risk of >20% for most of those aged over 75.[30] This increasingly important cohort of older individuals has been largely ignored by current primary prevention programmes, which focus on people under the age of 75. As the population ages, both statins and antihypertensive drugs offer the prospect of further reducing mortality and cardiovascular disease events, but only if they are prescribed.[10 31]

Strengths and weaknesses of the study

In this large study we used routine data from practices across the West Midlands and included all registered patients over the age of 40. For the purposes of this study, the West Midlands is representative of the national picture, having similar mortality rates in people aged ≥75 compared with the national picture (death rates in people aged 75-84 and in people aged ≥85 are 56.6 per 1000 and 152.7 per 1000, respectively, in England and Wales compared with 58.5 per 1000 and 157.6 per 1000 in the West Midlands).[32] The advantage of using this cohort over data from the Health Survey for England[33] is that the entire population from the study area was sampled and bias from differential response rates was not possible. In addition, we captured accurate data on all prescribed drugs over the preceding 90 days rather than having to rely on self reported accounts from participating patients, as was the case in the Health Survey for England.[33]

We included all patients in this analysis, regardless of their calculated cardiovascular risk. Given that age is the most significant factor in cardiovascular risk scores,[22 30] if we had done the analysis taking account of risk, the association of older age with non-use of preventive drugs would have been more marked. We did not do this as the risk calculators have been less well validated for people over the age of 75,[27 29] and true denominators would be difficult to establish as treatment with antihypertensive drugs and statins will lower calculated risk.

In estimating the proportion of patients receiving treatment, we could not account for contraindications to drug treatment, the general practitioner's judgment in individual cases, or patients' choice.[34] In addition, we could not distinguish between people who had never been offered primary preventive treatment and those in whom drug treatment was stopped, perhaps because of side effects or because of increasing age or frailty.

Study findings in the context of previous research

The "treatment-risk" paradox we observed, particularly for lipid lowering drugs, has been identified before in elderly patients eligible for secondary prevention.[11-14] The evidence supporting prescription of antihypertensive drugs in elderly patients is relatively well established. The HYVET study showed that antihypertensive treatment in independently living patients over the age of 80 with or without previous cardiovascular disease reduces risk of cardiovascular events and increases life expectancy.[31] Patients recruited to this trial were healthier than people of similar ages within the general population because of the strict exclusion criteria that restricted patients with multiple co-existing illnesses from participation.[35] Nevertheless, antihypertensive drugs are generally considered safe and effective in elderly patients, as reflected in guidelines in which recommendations on prescription of antihypertensive drugs are not restricted by age.[26]

The evidence for use of statins in the elderly is less clear.[36] The Heart Protection Study showed that treatment of people at high risk of cardiovascular disease of all ages (40-80) with simvastatin 40 mg results in a decreased risk of mortality from cardiovascular disease, coronary events, strokes, and revascularisations with no increased risk of mortality from non-cardiovascular disease or haemorrhagic stroke.[10] This effect was independent of age. The MEGA trial found a 33% risk reduction for coronary heart disease with no increase in non-cardiovascular disease mortality or other adverse events, and this effect was independent of age up to 80.[8] The ASCOT-LLA trial (in patients aged 40-79) found that statins reduce the risk of cardiovascular disease events and procedures (including fatal and non-fatal stroke),[9] and this effect was again independent of age.[37] The PROSPER trial, however, showed that while pravastatin given for three years reduced the risk of coronary disease in elderly individuals (aged 70-82), it had no effect on the risk of stroke.[38]

Despite evidence that supports the use of statins in patients up to the age of 80,[8-10 37 38] our findings suggest that general practitioners are choosing to follow guidelines[3] that recommend their use only up to age 74. Beyond 80, it is not clear whether statins are effective for primary prevention. This ambiguity exists not because of conflicting trial results, but because trials have not been conducted in this population.[39] There is no evidence to suggest that prescribing statins in elderly patients causes any increased side effects or adverse effects. The JUPITER trial found that (in patients aged 50-97), although adverse events were increased in older patients, there was no significant difference in such events between those taking statins and those taking placebo.[40 41]

In the absence of evidence from trials, guidelines rely on expert opinion.[3] Currently, while these guidelines note that statins are likely to be beneficial, they fall short of explicitly recommending them for the over 80s, and our findings suggest that general practitioners are not using them in most people of this age. Given the underlying risk associated with age[30 42] and that the protective effects of primary prevention drugs can be realised within just one year,[43] a case can be made for offering primary prevention to a larger proportion of people aged 80 and over than are currently receive it.

In contrast with previous research on secondary prevention[15 16] we found minimal clinically significant differences in prescription rates between men and women. This is perhaps surprising given that at any age men are at greater risk of a cardiovascular disease event than women.[30 42]

Implications for policy, research, and clinical practice

It is difficult to interpret whether the low use of preventive treatments (particularly statins) in older people reflects appropriate or inappropriate care. The non-use of these drugs might reflect a considered decision that has taken into account factors associated with age that might deter doctors from prescribing such as multiple comorbidity, polypharmacy, and cognitive decline as well as the patient's choice. There is only limited evidence of effectiveness, for statins at least, in people over the age of 80. Nevertheless, there is a striking contrast between use of statins and use of antihypertensive drugs in older people, which does point to possible underuse of statins. To better understand the clinical implications of our findings, more research is needed to determine why general practitioners refrain from prescribing primary preventive treatment in elderly people, the attitudes of older people towards preventive drugs, and the costs and benefits of prescribing in this age group. These are important questions to answer. The number of people aged 80 and over is projected to rise rapidly,[44] and greater use of these drugs might reduce disability and prolong healthy life expectancy in this age group.

Ultimately, evidence is needed to inform new guidelines that offer more precise recommendations on primary prevention for older people. In particular, consideration needs to be given to whether to continue to use an absolute risk based approach to guide treatment, whether there is a role for novel biomarkers to differentiate people who would benefit from treatment, or whether the optimal strategy might be to offer treatment to all people over a given age with fixed combination low dose multiple preventive drugs, otherwise known as the polypill approach.[22] It has been estimated that this could reduce the incidence of cardiovascular disease events by up to 80%.[22] The original polypill proposal suggested treating everyone over the age of 55, regardless of their absolute risk of cardiovascular disease.[22] Use of this strategy in people aged ≥75 could be an appropriate place to start, with a simple drug regimen that could reduce absolute risk with few adverse effects.[45]

Conclusions

Current guidelines[3] and screening strategies[46] for primary prevention of cardiovascular disease focus on people aged 40-74. Our study suggests that this is having an effect on the care of elderly patients aged ≥75. With continuing advances in healthcare, the elderly population is increasing and people are living to an older age.[44] They should therefore not be ignored by clinical trials and guidelines or overlooked in strategies for primary prevention of cardiovascular disease.

More research is needed to inform practice in primary prevention to deal with developing age inequalities and offer more specific advice about how best to treat elderly patients. Future research should test whether innovative treatment strategies, such as use of a polypill, could reverse these age inequalities in treatment of absolute risk of cardiovascular disease. There is a case for a simple trial of use of statins in people over the age of 80.

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What is already known on this topic

Antihypertensive drugs and statins are safe and effective treatments for absolute risk of cardiovascular disease

Age inequalities exist in prescription of statins for elderly patients with existing cardiovascular disease

What this study adds

Age inequalities also exist in those eligible for primary preventive treatment

Prescribing trends for statins seem to closely follow guidelines, which do not offer clear guidance for elderly patients

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Tables

Table 1| Characteristics of total population (by age group in years) potentially eligible for primary prevention treatment. Figures are numbers (percentages) unless stated otherwise

Characteristic	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	≥85
Total population	7035	6551	5447	4687	4695	3471	3089	2634	1917	1724
Patients with existing cardiovascular disease*	57 (1)	146 (2)	216 (4)	331 (7)	500 (11)	578 (19)	722 (23)	725 (28)	664 (35)	632 (37)
Primary prevention population*	6978 (99)	6405 (98)	5231 (96)	4356 (93)	4195 (89)	2893 (83)	2367 (77)	1909 (72)	1253 (65)	1092 (63)
Mean (SD) age (years)†	42 (1)	47 (1)	52 (1)	57 (1)	62 (1)	67 (1)	72 (1)	77 (1)	82 (1)	89 (4
Men†	3663 (52)	3288 (51)	2788 (53)	2153 (49)	2084 (50)	1331 (46)	1022 (43)	757(40)	456 (36)	293 (27)
Ethnicity:										
White‡	1974 (69)	1962 (74)	1678 (76)	1578 (81)	1617 (85)	1096 (82)	966 (79)	813 (79)	602 (87)	472 (90)
Black Afro-Caribbean‡	310 (11)	267 (10)	166 (8)	87 (5)	74 (4)	107 (7)	98 (8)	76 (7)	34 (5)	14 (3)
South Asian‡	461 (16)	297 (11)	301 (14)	217 (11)	156 (8)	(8) 44	118 (10)	85 (8)	25 (4)	27 (5)
Other‡	122 (4)	109 (4)	68 (3)	49 (3)	47 (2)	1556 (3)	44 (4)	49 (5)	29 (4)	565 (52)
Not stated†	4111 (59)	3770 (59)	3018 (58)	2466 (57)	2301 (55)	1556 (54)	1141 (48)	886 (46)	563 (45)	54 (52)
Current smoker†	1686 (24)	1598 (25)	1196 (23)	938 (22)	770 (18)	460 (16)	256 (11)	161 (8)	92 (7)	54 (5)
Blood pressure recorded†	5306 (76)	5310 (83)	4491 (86)	3840 (88)	3776 (90)	2672 (92)	2233 (94)	1787 (94)	1162 (93)	977 (89)
Cholesterol recorded†	2148 (31)	2559 (40)	2600 (50)	2395 (55)	2659 (63)	1998 (69)	1778 (75)	1385 (73)	935 (75)	672 (62)
Mean (SD of measured values)†:										
Systolic blood pressure (mm Hg)	126 (16)	130 (16)	132 (16)	135 (17)	137 (16)	138 (16)	139 (15)	140 (16)	142 (16)	141 (18)
Diastolic blood pressure (mm Hg)	79 (11)	81 (11)	81 (11)	81 (10)	80 (10)	79 (11	77 (11)	76 (10)	76 (10)	75 (11)
Cholesterol (mmol/L)	5.1 (1.0)	5.2 (1.0)	5.3 (1.0)	5.3 (1.1)	5.2 (1.1)	5.2 (1.1	5.1 (1.1)	5.0 (1.1)	5.0 (1.1)	5.2 (1.1)

*Proportion of total population within relevant five year age band.

†Proportion of primary prevention population within relevant five year age band.

‡Proportion of primary prevention population in whom ethnicity had been recorded.

Table 2| Likelihood of prescription of statins and antihypertensive drugs per five year increase in age (reference category was prescription rates in those aged 40-44)

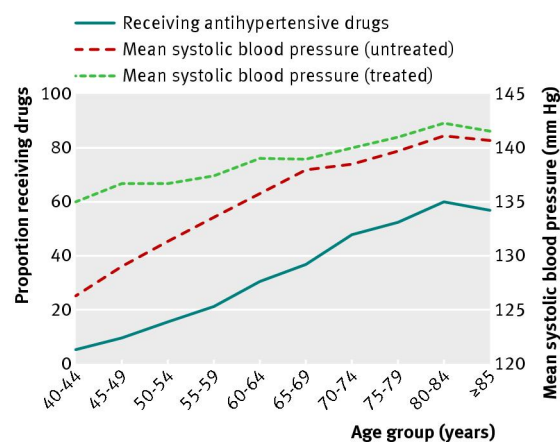| Age group (years)	Odds ratio (95% CI)*	
	Statins	Antihypertensive drugs
45-49	1.8 (1.5 to 2.1)	1.8 (1.6 to 2.0)
50-54	3.6 (3.0 to 4.3)	3.2 (2.8 to 3.7)
55-59	5.2 (4.4 to 6.2)	4.7 (4.2 to 5.4)
60-64	7.8 (6.7 to 9.2)	7.7 (6.8 to 8.7)
65-69	10.9 (9.3 to 12.9)	10.1 (8.9 to 11.5)
70-74	13.6 (11.5 to 16.1)	16.2 (14.1 to 18.4)
75-79	12.9 (10.8 to 15.3)	19.0 (16.6 to 21.8)
80-84	10.3 (8.5 to 12.5)	25.8 (22.2 to 30.1)
≥85	5.7 (4.6 to 7.2)	22.5 (19.2 to 26.3)

*All P<0.001.

Figures

Fig 1 Proportion of patients prescribed antihypertensive drugs and mean blood pressure of treated and untreated patients
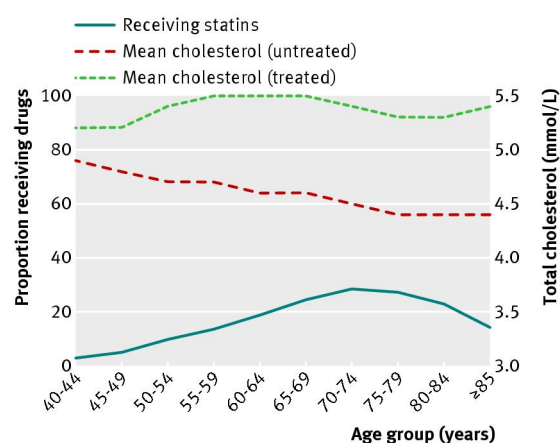

Fig 2 Proportion of patients prescribed cholesterol lowering drugs and mean cholesterol concentration of treated and untreated patients
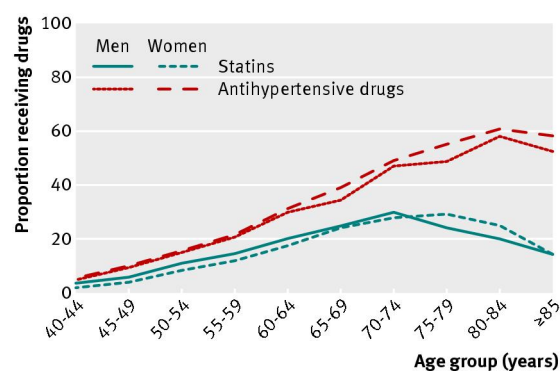

Fig 3 Proportion of patients prescribed primary preventive drug treatment in each age group by sex